



Covariate assessment of T-wave morphology and QTc prolongation

new opportunities in the evaluation of drug-induced ECG changes

Graff, Claus; Toft, Egon; Matz, J.; Kanthers, J. K.; Andersen, Mads Peter; Nielsen, J.; Struijk, Johannes

Publication date:
2010

Document Version
Early version, also known as pre-print

[Link to publication from Aalborg University](#)

Citation for published version (APA):

Graff, C., Toft, E., Matz, J., Kanthers, J. K., Andersen, M. P., Nielsen, J., & Struijk, J. (2010). *Covariate assessment of T-wave morphology and QTc prolongation: new opportunities in the evaluation of drug-induced ECG changes*. Abstract from Danish Cardiovascular Research Academy, Summer Meeting, Sandbjerg, Denmark.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal -

Take down policy

If you believe that this document breaches copyright please contact us at vbn@aub.aau.dk providing details, and we will remove access to the work immediately and investigate your claim.

Covariate Assessment of T-wave Morphology and QTc prolongation: New Opportunities in the Evaluation of Drug-induced ECG Changes

C Graff¹, E Toft¹, J Matz², JK Kanters³, MP Andersen¹, J Nielsen⁴, JJ Struijk¹

¹Aalborg University, Aalborg, DK, ²H. Lundbeck A/S, Copenhagen, DK

³University of Copenhagen, Copenhagen, DK, ⁴Aalborg Hospital, Århus University Hospitals, Aalborg, DK.

QTc prolongation due to the administration of a drug is not a reliable surrogate of the drug's proarrhythmic potential. Consequently, the development of suitable indices for the characterization of drug-induced repolarization changes might greatly improve risk assessment of new and existing compounds. This study adds a T-wave morphology composite score (MCS) to the QTc interval evaluation of drugs affecting cardiac repolarization.

Electrocardiographic recordings from 62 subjects on placebo and 400 mg moxifloxacin were compared to recordings from 21 subjects receiving 160 and 320 mg d,l-sotalol. The antibiotic drug, moxifloxacin has a favorable cardiovascular safety profile and is recommended as a positive control in thorough QT studies. In contrast, the antiarrhythmic drug d,l-sotalol has a less favorable safety profile with a reported incidence of TdP between 1.8% and 4.8%.

This difference in risk profiles between moxifloxacin and d,l-sotalol is indicated by T-wave morphology changes, as assessed by Δ MCS. T-wave morphology changes are larger for 320 mg d,l-sotalol than for 160 mg d,l-sotalol, which are again larger than for moxifloxacin and placebo. Covariate analyses of Δ QTc and Δ MCS showed T-wave morphology changes as a significant effect of dl-sotalol. In contrast, there is no effect of moxifloxacin on T-wave morphology (Δ MCS) at any given change in QTc.

This study offers new insights into the repolarization behavior of a drug with low cardiac risk versus a high risk drug and suggests added benefits of a T-wave morphology composite score as a covariate to the assessment of the QTc interval.

Corresponding author:

Claus Graff
Fredrik Bajers Vej 7 D1-215
9220 Aalborg Ø
Email: cgraff@hst.aau.dk
Phone: 61 33 33 69